REMARKS/ARGUMENTS

Applicants have amended Claims 1 and 12, to recite that the core sequence is based on receptor binding loops of VEGF-D only. Applicants have also amended Claim 12 to recite that the peptide produced by the method has certain biological activity, and cancelled Claim 13. Claim 23 has also been amended to remove subject matter subjected to restriction. Various dependent claims have been amended to replace the article "A" with "the," obviating the claim objections. Applicants respectfully submit that the amendments are fully supported by the application as originally filed. Entry of this amendment and favorable reconsideration of all claims are respectfully requested.

Claims 1-4, 12, 14-18, 23-26, 49-63, 72-103 are pending. Applicants note that Claim 52 is NOT withdrawn from consideration.

As noted above, the objections to claims 2-3, 13, 18, 50-55 and 63 for the usage of "A" instead of "The", and claim 23 for the recitation of subject matter not under consideration, have been obviated by the claim amendments.

Rejections under 35 U.S.C. §112 ¶ 1

"Lack of Enablement"

The Office Action continues to assert that the claims lacked enablement under 35 U.S.C. § 112, ¶ 1. Applicants respectfully traverse.

As an initial matter, Claim 1 has been amended to recite a monomeric monocyclic peptide based on a core sequence that consists of a receptor binding loop

VEGF-D. As a consequence, Claim 1 now recites a monomeric monocyclic peptide with a precisely defined structure (a loop sequence linked by two linking groups at either end) and a well-defined biological activity (interferes with the activity of VEGF, VEGF-C or VEGF-D).

The Office Action, in continuing to reject the claims, manifests misunderstandings of the law and the scope of the claims. First, in the second full paragraph on Page 3, the Office Action continues to focus on specific examples of peptides that did not show inhibitory activity. These non-inhibitory peptides, however, are OUTSIDE the scope of the claims. They are disclosed in the specification to demonstrate that it is easy and routine to screen for monocyclic peptides that actually show inhibitory effect. Furthermore, it is improper to state that some of the exemplified dimeric peptides are not *more* effective than some monomeric peptides, because the law does *not* require an invention to be more effective to be enabled.

The paragraph bridging pages 3 and 4 of the Office Action discusses "insufficient guidance" for a relationship between peptide structure and function. This is improper because as long as an ordinarily skilled person can practice (make or use) the claimed invention, it is irrelevant whether the mechanism or underlining principle of the invention is known or understood. The core sequence of VEGF-D receptor binding loop 1, 2 ,3 are very short (about 15 amino acid long). Conservative substitution or deletion of such a short peptides, coupled with well-known screening methods, requires only limited amount of effort for an ordinarily skilled artisan to make and use the invention as claimed, i.e. to obtain inhibitory monocyclic peptides

as claimed in Claim 1 without undue experimentation. In this regard, the Office Action's discussion of "addition" and "indefinite [sic, infinite?] number of monocyclic peptides" indicates that the examiner misunderstood the scope of the claim, because the claimed peptide comprises a core whose length and structure is finite and well-defined.

The discussion of the lack of *in vivo* data and the unpredictability of a pharmaceutical composition evinces again the use of an improper legal standard. The law does not require *in vivo* data for a patent claim to be allowable. See e.g. *In re Brana* 51 F.3d 1560, 1566 (Fed. Cir. 1995) (reversing the PTO decision based on finding that *in vitro* data did not support *in vivo* applications).

The Office Action seems to be extremely concerned with the use of the term "comprising," because a discussion thereof is repeated in the first full paragraph on Page 6 (and many times in subsequent parts of the Office Action). Applicants respectfully submit that the fact that it is open ended does not make a claim non-enabled. The legal standard is whether an ordinarily skilled person would be able to practice the claimed invention without undue experimentation, not whether the claim may theoretically encompass some extreme and non-functional "embodiments." For example, if a specification discloses a novel active pharmaceutical ingredient X, a claim of "A pharmaceutical composition comprising X and a suitable carrier" is enabled, even though the claim is open ended and theoretically encompasses a composition that also contains extremely toxic amount of arsenic. To an *ordinarily skilled person in the relevant art*, there is no need to engage in undue experimentation to practice the claimed invention. In this regard,

the fixation of the office action on an "infinite" number of amino acids that may theoretically be added to the loop (after it is circulized) is similary misplaced and improper.

"Lack of Written Description"

The Office Action also maintained the rejection of all pending claims for alleged lack of written description under 35 U.S.C. § 112, first paragraph. Applicants respectfully submit that the rejection related to the recitation of "loop 1, 2, and 3 of VEGF, and VEGF-C" (including the "new matter" rejection has been obviated by the above claim amendments. It is believed that the amendments, in addition to the above clarification of the claim scope, have also overcome the other reasons of the lack of written description rejection.

With regard to the "new matter" rejection related to the recitation of "first linking group... and second linking group," and "deleting at least one amino acid from said loop," the discussion in the Office Action indicates that the examiner has not considered applicants arguments at all. The Office Action merely repeated the assertion that "the applicants have not pointed out the support for said phrase." Quite to the contrary, applicants have specifically stated on page 14 of the response dated September 15, 2003 where support for the recitation can be found. Specifically,

> [A]pplicants respectfully submit that the phrase "first linking group at one end of the core sequence and second linking group at the other end of the core sequence" is mere re-wording, for

clarity purpose, of the description of the same meaning in the Specification (*see. e.g.* fifth to line on page 17 and line 9, page 19. *See also* Original claims 19 and 33: "cyclizing peptide loop fragments of said growth factor protein or corresponding loop fragments").

Finally, applicants submit that the same meaning of the phrase "deleting at least one amino acid from said loop prior to cyclizing the peptide" is conveyed at, *inter alia*, original Claim 9 ("deleting one or two internal amino acid residues from said loop fragment prior to cyclizing the peptide").

Accordingly, applicants respectfully request the "new matter rejections" be withdrawn.

Conclusion

Applicants respectfully submit that all claims are now in condition for allowance and solicit an early indication from the Examiner to this effect. If there are any questions regarding this amendment or the application in general, a telephone call to the undersigned would be appreciated since this should expedite the prosecution of the application for all concerned.

If necessary to effect a timely response, this paper should be considered as a petition for an Extension of Time sufficient to effect a timely response, and please

charge any deficiency in fees or credit any overpayments to Deposit Account No. 05-1323 (CAM #: 029065.48505US).

Respectfully submitted,

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